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(54) Title: REOVIRUS FOR THE TREATMENT OF CELLULAR PROLIFERATIVE DISORDERS

(57) Abstract

Methods for treating proliferative disorders, by administering reovirus to a Ras–mediated proliferative disorder, are disclosed. The reovirus is administered so that it ultimately directly contacts ras–mediated proliferating cells. Proliferative disorders include but are not limited to neoplasms. Human reovirus, non–human mammalian reovirus, and/or avian reovirus can be used. If the reovirus is human reovirus, serotype 1 (e.g., strain Lang), serotype 2 (e.g., strain Jones), serotype 3 (e.g., strain Dearing or strain Abney), as well as other serotypes or strains of reovirus can be used. Combinations of more than one type and/or strain of reovirus can be used, as can reovirus from different species of animal. Either solid neoplasms or hematopoietic neoplasms can be treated.

CLAIMS

What is claimed is:

1. A method of treating a ras-mediated proliferative disorder in a mammal, comprising administering to the proliferating cells in a mammal selected from dogs, cats, sheep, goats, cattle, horses, pigs, humans and non-human primates, an effective amount of one or more reoviruses in the absence of BCNU under conditions which result in substantial lysis of the proliferating cells.

2. The method of Claim 1, wherein the reovirus is selected from the group consisting of a mammalian reovirus and an avian reovirus.

3. The method of Claim 2, wherein the reovirus is a mammalian reovirus.

4. The method of Claim 3, wherein the reovirus is a human reovirus

5. The method of Claim 4, wherein the reovirus is selected from the group consisting of serotype 1 reovirus, serotype 2 reovirus and serotype 3 reovirus.

6. The method of Claim 5, wherein the reovirus is serotype 3 reovirus.

7. The method of Claim 2, wherein the reovirus is an avian reovirus.

8. The method of Claim 1, wherein more than one type of reovirus is administered.

9. The method of Claim 1, wherein more than one strain of reovirus is administered.

10. The method of Claim 1, wherein the reovirus is a field isolate.

11. The method of Claim 1, wherein the ras-mediated proliferative disorder is a neoplasm.

12. The method of Claim 1, wherein the ras-mediated proliferative disorder is neurofibromatosis.

13. The method of Claim 11, wherein the neoplasm is a solid neoplasm.

14. The method of Claim 11, wherein the neoplasm is selected from the group consisting of lung cancer, prostate cancer, colorectal cancer, thyroid cancer, renal cancer, adrenal cancer, liver cancer, pancreatic cancer, breast cancer and central and peripheral nervous system cancer.

15. The method of Claim 14, wherein the neoplasm is a central nervous system cancer.

16. The method of Claim 15, wherein the neoplasm is breast cancer.

17. The method of Claim 11, wherein the neoplasm is a hematopoietic neoplasm.

18. The method of Claim 13, wherein the reovirus is administered by injection into or near the solid neoplasm.

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19. The method of Claim 1, wherein the reovirus is administered intravenously into the mammal.

20. The method of Claim 1, wherein the reovirus is administered intraperitoneally into the mammal.

21. The method of Claim 1 wherein the mammal is immunocompetent.

22. The method of Claim 21 wherein the reovirus is immunoprotected.

23. The method of Claim 22 wherein the reovirus is encapsulated in a micelle.

24. The method of Claim 21 wherein the reovirus is administered along with an effective amount of an anti-antireovirus antibody.

25. The method of Claim 1, wherein the mammal is a human.

26. The method of Claim 1, wherein approximately 1 to 10^{15} plaque forming units of reovirus/kg body weight are administered.

27. The method of Claim 1, wherein the reovirus is administered in a single dose.

28. The method of Claim 1, wherein the reovirus is administered in more than one dose.

29. The method of Claim 11, wherein the neoplasm is metastatic.

30. The method of Claim 1 further comprising the administration of an effective amount of a chemotherapeutic agent, with the proviso that the chemotherapeutic agent is not BCNU.

31. A method of treating a ras-mediated proliferative disorder in a mammal selected from dogs, cats, sheep, goats, cattle, horses, pigs, humans and non-human primates, comprising administering to the proliferating cells an effective amount of one or more modified reoviruses under conditions which result in substantial lysis of the proliferating cells.

32. The method of Claim 11, wherein the reovirus is treated with a protease prior to administration.

33. A method of treating a ras-mediated neoplasm in a human, comprising administering to the neoplasm an effective amount of reovirus to result in substantial oncolysis of the neoplastic cells.

34. The method of Claim 33, wherein the neoplasm is a solid neoplasm and the reovirus is administered by injection into or near the neoplasm.

35. The method of Claim 34, wherein the solid neoplasm is pancreatic cancer.

36. A method of inhibiting metastasis of a neoplasm in a mammal, comprising administering to the neoplastic cells in a mammal selected from dogs, cats, sheep, goats, cattle, horses, pigs, humans and non-human primates, a reovirus in an amount sufficient to result in substantial lysis of the neoplastic cells.

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37. A method of treating a suspected ras-mediated neoplasm in a mammal, comprising surgical removal of the substantially all of the neoplasm and administration of a reovirus to the surgical site in an amount sufficient to result in substantial oncolysis of any remaining neoplastic cells.

38. A pharmaceutical composition comprising a reovirus, a chemotherapeutic agent and a pharmaceutically acceptable excipient with the proviso that the chemotherapeutic agent is not BCNU.

39. A pharmaceutical composition comprising a modified reovirus and a pharmaceutically acceptable excipient

40. The pharmaceutical composition of Claim 39 comprising an immunoprotected reovirus.

41. A kit comprising a pharmaceutical composition comprising a reovirus and a chemotherapeutic agent with the proviso that the chemotherapeutic agent is not BCNU.

42. A kit comprising a pharmaceutical composition comprising a reovirus and an anti-antireovirus antibody.